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YOUNG & THOMPSON  
209 Madison Street  
Suite 500  
Alexandria, VA 22314

EXAMINER
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CRAIGO, WILLIAM A

ART UNIT	PAPER NUMBER
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1615

NOTIFICATION DATE	DELIVERY MODE
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12/03/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/591,131	<b>Applicant(s)</b> ROYERE ET AL.	
	<b>Examiner</b> WILLIAM CRAIGO	<b>Art Unit</b> 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 21-40 is/are pending in the application.
- 4a) Of the above claim(s) 39 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21,25-31,34-36 and 38 is/are rejected.
- 7) ☒ Claim(s) 22-24 and 37 is/are objected to.
- 8) ☒ Claim(s) 39 and 40 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of the Application***

The remarks and amendments filed on 24 August, 2009 are acknowledged.

Claims 21-40 are pending in this application

Claims 21, 22, 25, 32, 33, 38 and 39 have been amended.

### ***Election/Restrictions***

Newly submitted claims 39 and 40 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Originally presented claims 39 and 40 were un-examinable for art purposes because they were directed to a method without any recitation of a positive step.

. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

**Group I**, claim(s) 21-38, drawn to a method of preparing microspheres.

**Group II**, claim(s) 39-40, drawn to a method of treatment/administering.

As set forth in Rule 13.1 of the Patent Cooperation Treaty (PCT), "the international application shall relate to one invention only or to a group of inventions so

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linked as to form a single general inventive concept." Moreover, as stated in PCT Rule 13.2, "where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." Furthermore, Rule 13.2 defines "special technical features" as "those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Groups I-II is a method of preparation of monodisperse biodegradable microspheres. The method of preparation of monodisperse biodegradable microspheres of claim 1 does not present a contribution over the prior art. As disclosed in Collins, WO 03/106809 Example 2 and claim 1, the method of preparation of monodisperse biodegradable microspheres of instant claim 1 is not novel. As such, Group I does not share a special technical feature with the instant claims of Group II. Therefore, the claims are not so linked within the meaning of PCT Rule 13.2 so as to form a single inventive concept, and unity between Groups I-II is broken.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Response to Arguments***

#### **Withdrawn Rejections**

##### **Rejection of claims under 35 USC § 112:**

In view of applicant's amendments, the rejection of claims 39-40 under 112 2nd is withdrawn.

In view of applicant's amendments, the rejection of claim 25 under 112 2nd is withdrawn.

##### **Rejection of claims under 35 USC § 101:**

In view of applicant's amendments, the rejection of claims 39-40 under 101 is withdrawn.

#### ***New Rejections***

Applicant's arguments with respect to claims 21-40 have been considered but are moot in view of the new ground(s) of rejection.

### ***Claim Objections***

Claims 22-24 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 22 recites " . . . wherein the majority of the microspheres are constituted in majority by the biodegradable polymer." As the parent claim 21 has been amended to include the limitation of biodegradable polymer, claim 22 no longer further limits claim 21 and is improper. Claims 23-24, dependent on claim 22 are rejected as being dependent on an improperly dependent claim.

Applicant is advised that should claim 32 be found allowable, claim 33 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim 37 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 37 recites "...wherein the step of calibration by laminar shearing is carried out in a

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Couette device"; however as there is no step reciting "calibration" in claim 21, therefore claim 37 fails to further limit parent claim 21 and is improper.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, claim 21 recites the limitation of "controlled laminar shearing"; this phrase does not appear to have a definition in the specification and is not defined in the context of the claim. One of ordinary skill is not reasonably apprised of what applicant considers their invention, it is not clear from the language of the claim or the specification what applicant does or does not consider their invention, i.e. the metes and bounds of the invention are not clearly laid out.

Claims 32 and 33 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, claims 32 and 33 recite "...wherein the organic phase of the emulsion comprises from 1 to 50%"; however, the claim does not indicate whether this is 1 to 50% by volume or weight.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 21, 25-28, 31, 34-36 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Collins, WO 03/106809 A1, 24 December, 2003.

Collins is directed to the preparation of chemicals encapsulated in a continuous polymeric phase (i.e. a microsphere) comprising a degradable polymer.

Example 2 and claim 1 of Collins describes the steps of preparing an emulsion comprising an organic phase with an active ingredient (a water soluble or water dispersible oil, water dispersible means that there is an organic phase separate from the aqueous phase), and a degradable polymer (example 2 teaches polylactide-co-glycolide, a biodegradable polymer) and an aqueous phase. Collins does not teach the recited viscosity; however, since the composition of the emulsion taught in Collins appears to be the same and prepared in the same manner as recited in instant claim 21, it is reasonable to conclude that the composition taught in Collins inherently possesses the viscosity ratio claimed because compound inherent properties are immutable. Thus the burden is shifted to applicant to provide objective evidence to show that the emulsion as taught by Collins does not inherently possess the viscosity ratio claimed. See MPEP 2112, V.



Example 2 teaches high shear mixing, then dispersing the emulsion in an aqueous phase/allowed to stir overnight (meeting the limitation of removing the organic solvent), and isolating the microparticles (i.e. microspheres, Collins, claim 5).

Collins anticipates the subject matter of instant claim 21.

Collins, example 2 teaches the biodegradable polymer with a molecular weight of 65,000 daltons anticipating the range recited in claim 25.

Collins, claim 9, teaches ethyl acetate anticipating instant claim 26.

Collins, claim 1, teaches a water-dispersible oil as an active ingredient therefore meeting the limitation of lipid soluble, anticipating instant claim 27.

Collins, claim 1 teaches a water-soluble oil as an active ingredient anticipating instant claim 28.

Collins, example 2, pg. 31 teaches a double emulsion wherein the organic phase represents roughly 30% (15g (10ml dichloromethane)/ 50g (50ml aqueous phase)) anticipating instant claims 31 and 34.

Collins, example 2 teaches an external aqueous phase with a stabilizing agent (polyvinyl alcohol) anticipating instant claims 35 and 36.

Collins, example 2, teaches the dilution of the primary emulsion by 50ml of an aqueous solution of polyvinyl alcohol and Tween 80, effectively extracting the organic solvent into the aqueous phase. The microparticles are then washed with 300ml aliquots of water during recovery of the microparticles. The reference teaches removing the solvent from the organic phase by extraction in water anticipating instant claim 38.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 21, 25-28, 31, 34-36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1, 24 December, 2003 in view of Lobo, US 5589322 A, 31 December, 1996.**

Collins does not explicitly teach the emulsion has a ratio of organic to aqueous phase viscosity in the range of 0.1 to 10; however, Lobo teaches (examples 1-3) viscosity ratios,  $q$ , listed in the tables, between 0.1 and 10. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the known technique of modifying the viscosity ratio of organic to aqueous phases as taught in Lobo to improve the emulsion method of Collins to produce monodisperse microspheres because Lobo teaches the viscosity ratio is correlated to the particle size produced, i.e. by adjusting the viscosity ratio, one can adjust the size of the microspheres produced. Thus Collins teaches a method of producing a monodisperse population of microspheres and Lobo teaches a method of controlling the size of the microspheres produced. By modifying the method of Collins with the viscosity ratio as taught in Lobo one of ordinary skill is able to provide a monodisperse population of microspheres of a predictable size. Accordingly, the claimed invention of claims 21, 25-28, 31, 34-36 and 38 was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

**Claims 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins, WO 03/106809 A1, 24 December, 2003 in view of Lobo, US 5589322**

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**A, 31 December, 1996 as applied to claims 21, 25-28, 31, 34-36 and 38 above, and further in view of Okada, US 5643607, 1 July, 1997.**

Neither Collins nor Lobo disclose an active ingredient which is a peptide or protein (instant claim 29), nor a hydrophilic active ingredient in combination with a lipophilic active ingredient (instant claim 30).

Okada teaches the delivery of polypeptides from microcapsules (i.e. microspheres) prepared by a water in oil emulsion (abstract). The physiologically active peptides disclosed by Okada, col. 2, line 17-67 include proteins (two or more amino acid residues and a molecular weight of about 200 to 100,000, insulin etc.). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute the physiologically active peptides as taught in Okada for the active ingredients taught in Collins with the modified viscosities as taught by Lobo to obtain the predictable result of providing monodisperse microspheres as in instant claim 29 because all of the documents are directed to solving the problem of providing microparticles by emulsion technology. Further a protein is comprised of hydrophilic active ingredients in combination with lipophilic active ingredients because proteins are made up of amino acids some of which are hydrophilic, for example arginine, and some are lipophilic, for example phenylalanine. Since amino acids are active ingredients in and of themselves and proteins are combined amino acids the proteins taught in Okada meet the limitation of a hydrophilic active ingredient in combination with a lipophilic active ingredient as recited in instant claim 30. Accordingly, the claimed invention of

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claims 29 and 30 was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to WILLIAM CRAIGO whose telephone number is (571)270-1347. The examiner can normally be reached on Monday - Friday, 7:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

William Craigo

/Leon B Lankford/

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Primary Examiner, Art Unit 1651